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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,892	03/21/2005	Yoshiyuki Ueno	IPE-051	9982

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EXAMINER	
SYKES, ALTREV C	
ART UNIT	PAPER NUMBER
1794	
MAIL DATE	DELIVERY MODE
10/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,892	UENO ET AL.	
	Examiner	Art Unit	
	ALTREV C. SYKES	1794	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17, 19-40* is/are pending in the application.

4a) Of the above claim(s) *19-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 18, 2009 has been entered.

Response to Amendment

2. The amendment to the claims filed August 18, 2009 is acknowledged by examiner and has been entered. Claims 1, 10 and 16 have been amended. Claims 1-17 and 40 are pending examination on the merits.

Response to Arguments

3. Applicant's arguments, see pg.2, filed August 18, 2009, with respect to the discussion of polymethyl methacrylate in relation to the Kasai et al. prior art have been fully considered and are persuasive.

4. Applicant's arguments filed July 20, 2009 with respect to claims 1-17 and 40 have been considered but are moot in view of the new ground(s) of rejection necessitated by amendment for the limitation of covalently bonded.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-5, 7-17 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kasai et al. (US 4,776,959) in view of Shimagaki et al. (US 5,938,929)

Regarding claims 1, 15 and 40 Kasai et al. discloses a porous membrane of a hydrophobic polymer and a coating formed on at least one surface of the porous membrane and on the inner surface of the pores of the porous membrane with a water-insoluble hydrophilic polymer soluble in a solvent exhibiting satisfactory stability and a satisfactory wetting property with respect to the hydrophobic polymer mentioned above. (See Col 2, lines 35-51 and Col 3, lines 15-25)) Examiner equates the porous hydrophobic membrane of Kasai et al. to the precursor substrate as claimed by applicant. Kasai et al. discloses that the water-insoluble hydrophilic polymer may include vinyl alcohol-vinyl acetate copolymer. (See Col 4, lines 50-53) Kasai et al. also discloses optionally, the vinyl alcohol-vinyl acetate copolymer may be cross-linked and further insolubilized. (See Col 6, lines 38-42)

Regarding the limitation that the hydrophilic polymer be covalently bonded to the precursor surface, examiner notes that applicant provides the Shimagaki reference to

teach that irradiating the substrate with radiation would inherently result in covalent bonding as well as crosslinking. (See pg. 12 remarks filed July 20, 2009) As such, examiner notes that specifically Shimagaki et al. discloses it is possible to cross-link the hydrophilic polymer and thus make it insoluble by radiation and/or heat. (See Col 11, lines 37-38) Shimagaki et al. discloses radiation of gamma-rays or electron beams produces covalent bonds with the polymer materials, and the dissolution of the hydrophilic polymer is checked. In the case of the heat treatment, the hydrophilic polymer itself gels into a higher molecule and insoluble form. (See Col 11, lines 44-49)

As Kasai et al. and Shimagaki et al. are both directed to membranes for use in artificial kidneys, the art is analogous. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the process of crosslinking as taught by Shimagaki et al. for the crosslinking process as disclosed by Kasai et al. motivated by the desire to provide an insoluble hydrophilic polymer on a hydrophobic membrane substrate thereby providing safety of the product when used for medical purposes. (See Col 11, lines 33-36 and 63-66)

Regarding the limitation of the ratio of hydrophilic polymer not covalently bonded to the surface of the precursor substrate to the total amount of the hydrophilic polymer of the modified substrate, Kasai discloses that the concentration of the hydrophilic polymer in the solution is generally in the range of 0.1 to 10.0% by weight, although it is variable with the average pore diameter possessed by the porous membrane of the hydrophobic

polymer subjected to the treatment of impregnation. (See Col 5, lines 25-31) Kasai et al. also discloses that the amount of hydrophilic polymer is preferably in the range of 0.05 to 1 parts by weight per 100 parts of the hydrophobic polymer. (See Col 5, lines 55-58) Therefore, examiner notes that the hydrophilic polymer is used in an amount of less than 15% by weight in solution for the impregnation of the membrane. Therefore Kasai anticipates a membrane wherein some of the hydrophilic polymer is not covalently bonded to the surface of a membrane since the hydrophilic polymer is deposited on the inner surface of the pores of the membrane as well as the surface. Regarding the limitation that the number of adhered human blood platelets is $10/4.3x10^3$ μm^2 or less when the modified substrate is brought into contact with human blood which contains heparin with a concentration of 50 U/mL at 37° C for one hour. It is noted by examiner that heparin is a component added to human blood as an anticoagulant, therefore, the number of adhered blood platelets would be minimal since the whole idea of adding the compound is to avoid clotting of the platelets. Additionally, Kasai discloses a membrane capable of use for artificial organs such as artificial kidney and blood plasma separation. (See Col 6, lines 43-50) Kasai discloses in the final filter, true fungi, bacteria, and microfine particles entrained by the transfusion fluid are stopped by the hydrophilic porous membrane. Therefore, only the cleaned transfusion fluid is passed through the filter thereby suggesting to one of ordinary skill in the art that substantially no blood platelets would adhere to the substrate when placed in the conditions as claimed by applicant.

Regarding claims 2 and 4 Kasai et al. also discloses optionally, the vinyl alcohol-vinyl acetate copolymer (hydrophilic polymer) may be cross-linked and further insolubilized. (See Col 6, lines 38-42) Shimagaki et al. discloses it is possible to cross-link the hydrophilic polymer and thus make it insoluble by radiation and/or heat. (See Col 11, lines 37-38) Further, as the structure and composition of modified Kasai et al. has been shown to be similar to that of the structure and composition as claimed by Applicant, it is presumed that the prior art can do whatever is claimed since the similarity is substantial. As such, it is noted that the modified substrate of Kasai et al. is also capable of being obtained by irradiating with radiation while the substrate is brought into contact with an aqueous solution of the hydrophilic polymer and even further with an antioxidant.

Regarding claims 3 and 5 modified Kasai teaches the claimed invention above. While the reference does not explicitly disclose the modified substrate wherein in the aqueous solution of the hydrophilic polymer, the maximum increasing value of ultraviolet absorption value in the wavelength range of 260 to 300 nm, the increase being caused by irradiating with radiation, is 1 or less, it is reasonable to presume that the maximum increasing value is readily expected in view of modified Kasai. Support for said presumption is found in the use of like materials and/or like methods which would result in the claimed property. In the instant case, modified Kasai et al. discloses a modified substrate comprising a hydrophilic polymer which is capable of being made by irradiating with radiation as set forth above. Additionally, the maximum increasing value as claimed

is 1 or less wherein less is understood to encompass zero and the limitation is therefore a case of prima facie obviousness exists.

Regarding claims 10, 13 and 14 modified Kasai teaches the claimed invention above. While the reference does not explicitly disclose the modified substrate wherein in the amount of dissolution of the hydrophilic polymer is 0.5 mg/m^2 or less, and does not explicitly disclose the modified substrate wherein in the adsorptivity to interleukin-6 is at least 0.1 ng/cm^2, it is reasonable to presume that the amount of dissolution is inherent to Kasai. It is also reasonable to presume that the immobilization density of the polyalkylene glycol is 150 to 3,000 mg/m^2 would be readily expected in view of modified Kasai et al. since it has been shown that Kasai et al. discloses a membrane substantially similar in choice of hydrophilic polymer and the final use of the product substrate which would result in the claimed property. Support for said presumption is found in the use of like materials and/or like methods which would result in the claimed property. In the instant case, Kasai et al. discloses a modified substrate comprising a hydrophilic polymer which excels in properties such as resistance to heat and resistance to chemicals. (See Col 3, lines 40-46) Kasai et al. also discloses that the porous membrane encompasses a hydrophilic polymer in a solvent exhibiting a satisfactory ability to dissolve the hydrophilic polymer and possessing high stability and a high wetting property with respect to the hydrophobic polymer. (See Col 4, lines 25-32) Additionally, the amount of dissolution as claimed is 0.5 mg/m^2 or less wherein less is understood to encompass zero. Modified Kasai et al. discloses a modified substrate similar in composition to that of the

applicant. Furthermore, Kasai et al. discloses that the hydrophilic porous membrane finds utility as a final filter for medicinal liquids and transfusion liquids, pharmaceutical filters, and membranes for artificial organs such as artificial kidney and blood plasma separation. (See Col 6, lines 43-53 and Figure 2) As such, the claimed properties would have been obvious in view of the combined teachings.

Regarding claim 7 Kasai et al. also discloses that it may be favorable to vary the strength of a porous membrane and obtain a hydrophilic membrane answering the purpose of its use by simultaneously incorporating therein an additional polymer such as polymethyl methacryalte which as satisfactory affinity for the hydrophobic polyvinyl fluoride and is capable of enhancing the hardness of the resin. (See Col 6, lines 30-37) Kasai et al. discloses the hydrophilic porous membrane of this invention finds utility in various applications because it excels in perviousness to water, efficiency of filtration, and mechanical strength. (See Col 6, lines 43-46)

Shimagaki et al. discloses the membrane for artificial kidneys preferably comprise a stock solution comprising a 4 component system of (1) polysulfone resin, (2) hydrophilic polymer, (3) solvent, and (4) additive. (See Col 3, lines 40-46) Shimagaki et al. discloses that the hydrophilic polymer (2) is a polymer having compatibility with the polysulfone resin. Polyvinyl pyrrolidone is most desirable, but other polymers which may be present additionally may include poly(vinyl acetate). (See Col 3, lines 61-67)

Therefore, the use of a plurality of hydrophilic polymers would have been obvious to one of ordinary skill in the art at the time of the invention motivated by expected success since the both prior art references acknowledge the use of more than one hydrophilic polymer thereby tailoring the properties of the membranes for intended use.

Regarding claims 9 and 11 applicant discloses nonionic hydrophilic polymers such as polyalkylene glycols and polyvinylpyrrolidone provide an inhibiting effect of nonspecific adsorption. Anionic polymers such as dextran sulfate and polyvinyl sulfate provide an excellent inhibiting effect of adsorption of basic substances such as lysozyme. In terms of a high inhibiting effect of adsorption, polyalkylene glycols such as polyethylene glycol and polypropylene glycol or polyvinylpyrrolidone is particularly preferable. (See [0029]) Kasai et al. discloses when the hydrophobic polymer is polyvinylidene fluoride, for instance, such hydrophilic polymers examples include vinyl alcohol-vinyl acetate copolymers, random and block copolymers of vinyl pyrrolidone such as vinyl acetate-vinyl pyrrolidone copolymer, polyethylene glycol block copolymers such as polymethyl methacrylate-polyethylene glycol block copolymer, segmented polyurethane having polyethylene glycol as a soft segment thereof, and block and random polyamino acids combining hydrophilic amino acids (wherein an organic residue except amino group is hydrophilic) with hydrophobic amino acids (wherein an organic residue except amino group is hydrophobic). (See Col 4, lines 37-49) As set forth above, Kasai et al. also discloses that it may be favorable to vary the strength of a porous membrane and obtain a hydrophilic membrane answering the purpose of its use by simultaneously incorporating

therein an additional polymer such as polymethyl methacryalte which as satisfactory affinity for the hydrophobic polyvinyl fluoride and is capable of enhancing the hardness of the resin. (See Col 6, lines 30-37)

Therefore, it would have obvious to one of ordinary skill in the art to modify the type of hydrophilic polymers used motivated by the desire to tailor the properties of the resin to end product use. (See Col 6, lines 30-37)

Regarding claims 16 and 17 examiner maintains the position as set forth above for claims 1 and 13. Kasai further discloses typically, main uses found for the membrane are final filters for medicinal liquids and transfusion fluids, pharmaceutical filters, and membranes for artificial organs such as artificial kidney and blood plasma separation. (See Col 6, lines 46-50)

Regarding the limitation that the hydrophobic polymer comprise polymethylmethacrylate, examiner notes that Shimagaki et al. discloses that as a material of the membrane for dialyzers, there were conventionally used a number of polymeric compounds such as cellulose acetate, and poly (methyl methacrylate). (See Col 1, lines 8-11)

As such, it would have been obvious to one of ordinary skill in the art at the time of the invention motivated by expected success to utilize the conventional membrane of poly(methyl methacrylate) since the prior art teaches that it is favorable in producing

dialyzers and the membranes of the combined prior art would be utilized in the same manner.

7. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kasai et al. (US 4,776,959) in view of Shimagaki et al. (US 5,938,929) as applied to claim 1 above in view of Graiver et al. (US 5,429,839)

Regarding claim 6, Kasai et al. discloses all of the claim limitations as set forth above but the reference does not disclose the surface hydrophilic polymer ratio is at least 20 weight percent.

Graiver et al. discloses an aqueous coating composition for solid substrates formed from hydrophobic polymers, said composition comprising a solubilized hydrophilic organic polymer. (See Col 4, lines 9-28) Graiver et al. discloses polyvinyl alcohol is a preferred hydrophilic polymer based on the cost and availability of this material. (See Col 4, lines 59-60) Graiver et al. discloses the useful upper limit for the concentration of polyvinyl alcohol is determined at least in part by the viscosity of the solution and the capabilities of the equipment used to prepare the solution and coat it on the substrate. (See Col 5, lines 35-38) Graiver et al. discloses using the preferred molecular weight range of from 80,000 to 115,000 the upper limit of polymer concentration appears to be 20 weight percent. (See Col 5, lines 39-41) Graiver discloses that substrates coated in such a way are suitable for artificial implants and other medical devices. (See Col 6, lines 42-52)

As both modified Kasai et al. and Graiver et al. are both directed to hydrophilic polymer and hydrophobic substrates, the art is analogous. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention motivated by expected success to utilize the weight percent of hydrophilic polymer as taught by Graiver et al. for the hydrophilic polymer on the surface of the substrate as taught by Kasai et al. since Graiver discloses that substrates coated in such a way are suitable for artificial implants and other medical devices. (See Col 6, lines 42-52)

8. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kasai et al. (US 4,776,959) in view of Shimagaki et al. (US 5,938,929) as applied to claim 7 above in view of Nagatomo et al. (US 5,023,052).

Regarding claim 8, Kasai et al. discloses all of the claim limitations as set forth above. Kasai further discloses the hydrophilic polymer may be vinyl acetate-vinyl pyrrolidone copolymer which is noted to be nonionic. (See Col 5, lines 9-23) Kasai discloses that an additional polymer may be used. (See Col 6, lines 30-37) The reference does not disclose the substrate comprises a cationic hydrophilic polymer and a nonionic hydrophilic polymer.

Nagatomo et al. discloses an element for dry chemical analyses useful for quantitative determination of a specific substance in body fluids, such as blood. (See Col 1, lines 5-7)

The analytical element may have various layer structures, for example a layer structure (1) comprising a support having provided thereon the first non-fibrous porous layer, the second non-fibrous porous layer. (See Col 5, lines 25-30) Additionally, Nagatomo et al. discloses a layer structure (2) comprising a support having provided thereon an adhesive layer (or water absorbing layer). (See Col 5, lines 30-35) A third structure taught by Nagatomo et al. comprises a support having provided thereon a detecting layer which generally comprises a hydrophilic polymer and may contain a mordant, for example a cationic polymer mordant. (See Col 48-58)

As both Kasai et al. and Nagatomo et al. disclose products useful in blood plasma separation, the art is analogous. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention motivated by expected success to utilize a cationic polymer as taught by Nagatomo et al. as the additional on the substrate of Kasai et al. having a nonionic polymer thereon for the added benefit of enhancing the separation substrate to analyze a specific component in whole blood, thereby giving a highly precise result irrespective of the hematocrit value of the blood. (See Col 2, lines 54-61)

9. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kasai et al. (US 4,776,959) in view of Shimagaki et al. (US 5,938,929) as applied to claim 1 above in view of Ricketts et al. (US 2,715,091).

Regarding claim 12 modified Kasai et al. discloses all of the claim limitations as set forth above but the reference does not disclose the hydrophilic polymer is a polymer derived from the living body. It is noted that applicant discloses that examples of hydrophilic polymers derived from the living body include dextran and dextran sulfate. (See [0030])

Ricketts et al. discloses anticoagulants for use with blood and plasma which are non-toxic and may be readily prepared on a large scale. (See Col 1, lines 18-21) Ricketts et al. also discloses a water soluble salt of dextran sulphate as a anticoagulant which like heparin may be successfully employed after blood has been shed "in vitro" or used within the body "in vivo". (See Col 1, lines 44-46 and Col 2, lines 17-22)

As modified Kasai et al. discloses a hydrophilic porous membrane which can be used as a final filter for blood plasma transfusion and Ricketts et al. also discloses the manufacture of anticoagulants for use with blood and plasma, the art is analogous. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the anticoagulant dextran sulphate of Ricketts et al. as the hydrophilic polymer on the substrate of Kasai et al. in order to produce a final membrane that would prevent blood from clotting while the membrane was being used as a final filter for a transfusion. One of ordinary skill in the art would have been motivated by expected success since it is recognized by Ricketts that dextran sulphate can be produced in large quantities and at low cost. (See Col 1, lines 63-66)

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALTREV C. SYKES whose telephone number is (571)270-3162. The examiner can normally be reached on Monday-Thursday, 8AM-5PM EST, alt Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Tarazano can be reached on 571-272-1515. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D. Lawrence Tarazano/
Supervisory Patent Examiner, Art Unit 1794

/ACS/
Examiner
10/90/09